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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/390,634	09/07/1999	PAUL J. PRICE	0942.4190002	7270

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STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/390,634	PRICE ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *176-282* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *176-282* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 September 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a divisional of application 08/781,772, filed January 10, 1997, now abandoned.

Applicants' amendment filed November 17, 2004, has been received and entered. Claims 1-175 have been cancelled. Claims 176-282 have been added. Claims 176-282 are pending and currently under examination.

Information Disclosure Statement

The information disclosure third supplemental statement (IDS) submitted on January 11, 2005, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

It is noted that Bodnar *et al.* (US Patent 6,800,480) teaches compositions and methods for culturing embryonic stem cells, however every specific example within the specification clearly indicates that serum is added to the medium for culturing.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 176-180, 182-192, 194-, 214, 216-282 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition of mouse

embryonic stem cells and serum-free media capable of preventing differentiations of mouse embryonic stem cells, and the methods of use of said composition, does not reasonably provide enablement for other combinations of media and embryonic stem cells from any other animal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. .

The courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in patent application. 27 USPQ2d 1662 *Ex parte Maizel*. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case the claims broadly encompass any serum-free media and an embryonic stem cell from any animal, with the caveat that the media will prevent the differentiation of the embryonic stem cell in culture. The specification provides guidance for the components of a synthetic serum (see for example Tables 1-3), however none of the instant claims recite the use of a serum supplement. The present specification provides several working examples using mouse embryonic stem cells. At the time of filing, multiple mouse embryonic stem cell lines had been established, however embryonic stem cells from other animals were not. While attempts to isolate embryonic stem cells from other species were made, at the time of filing, it was apparent that the methods used to obtain and culture mouse embryonic stem cells could not simply be used for other species. Subsequently, for human embryonic stem cells it was demonstrated that the failure of previous attempts was due the unique requirements of human cells, notably the inability of LIF to affect differentiation and the requirement of a fibroblast feeder layer for human cells. The present claims encompass and specifically recite compositions of stem cells from animals from which the embryonic stem cell has yet to be isolated. While it is generally believed that all animals have stem cells, and the are present at the early stage of embryogenesis, similar to the attempts to isolate human embryonic stem cells, embryonic stem cells from other species have not been isolated because the specific conditions for culturing them and each of their unique characteristics and properties have not been defined. The present specification provides guidance for making a synthetic serum supplement to substitute for serum, and demonstrate that this is effective in culturing mouse embryonic stem cells. However, the guidance of the present specification fails to provide a nexus between these teachings and what is encompassed by the claims. Importantly, as noted above, the present

claims encompass embryonic stem cells that have not been isolated successfully to date. Providing guidance to a synthetic serum supplement fails to provide the necessary guidance required to obtain the breadth of the claimed compositions. The methods of use of the compositions are included in the basis of the rejection because they require the claimed compositions to practice. It would not be contested that once the particular species of cell was isolated and characterized, it could be used in well established methods such as for producing a protein of interest or as in the art of transgenics, however since the cells have not been isolated one can not use these cells in any method.

In view of the quantity of experimentation necessary to determine the parameters listed above, the lack of direction or guidance provided by the specification, the absence of working examples for the demonstration or correlation to the production of embryonic stem cells from other animals and the appropriate media for preventing differentiation, and the general unpredictable state of the art with respect to the isolation and properties of the resulting embryonic stem cell with its unique properties and requirements needed to maintain it in an undifferentiated state, it would have required undue experimentation for one skilled in the art to make and/or use the claimed inventions as broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims previously rejected under 35 U.S.C. 102(b) as being anticipated by Ponting (US Patent 5,405,772) have been cancelled.

To the extent the teachings of Ponting would apply to the instant claims, it is noted that Ponting provides clear and specific guidance to generate a synthetic serum supplement to make a complete media, and the general teachings of the components would anticipate the general teachings of the instant specification as set forth in the previous office actions. However, Ponting does not provide the specific media requirements nor the specific methods to test the affect of a serum supplement on differentiation of embryonic stem cells. Though Ponting does teach to use the complete media for culturing embryonic stem cells, and specifically refers to stem cells known in the art at the time of filing, the specification fails to teach the particular combination of components important in preventing differentiation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Newly added claims 176-282 are rejected under 35 U.S.C. 103(a) as obvious over Ponting (US Patent 5,405,772), Gibco BRL Products and Reference Guide ((1997) Chapters 5 and 8) and Atsumi *et al.* (Develop. Growth & Differ. 35(1):81-87 (1993)).

It is noted that claims have been effectively amended to encompass any basal serum-free media to one that is a serum-free media capable of "preventing differentiation of the embryonic stem cells during expansion" (see new claim 176 compared to cancelled claim 89). As noted in the previous office action, Atsumi *et al.* provides evidence that at the time of filing and issuance of Ponting serum-free conditions for culturing embryonic stem cells were known and used. Atsumi *et al.* teach to use as a serum supplement serum-free media that are obtained as a conditioned media. Using such media Atsumi *et al.* were able to define specific factors supplied by the feeder cells in order to make a complete serum-free media. As noted previously, the teaching of Ponting anticipates the specific embodiments required to make a synthetic serum supplement. It is noted that Ponting does not specifically disclose all the specific components listed in the claims, however the use of these components would be obvious because they are factors commonly used in cell culture. Further, Ponting teaches that the media should be as defined as possible and optimized for a given cell type, therefore one would be motivated to use and test the various forms of these components for their specific affects on the cells in culture. For example lipid-poor albumin provides a more delined source of albumin, lacking lipids that could affect the cells. Moreover, Ponting teaches that the components can be synthetic (column

11, lines 65-68), wherein a synthetic component would represent a more defined molecule free from potential contaminants that may be present in naturally isolated sources. The level of knowledge and skill in the art for culturing cells is high, and there would be a reasonable motivation and expectation of success to use specific components from various sources as generally taught by Ponting to provide for a more defined and optimized media. Upon review of the present specification, there is no specific teaching that any one of the components recited or encompassed by the instant claims provides any unexpected affect on the cultured cells that would not have been readily known in the art, such as the use of LIF or feeder cells to maintain embryonic stem cells in culture.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

Joe Woitach
AU1632